Amendments to the Claims

Applicants acknowledge and wish to thank the Examiner for the withdrawl of the previous restriction requirement.

Please amend claims 1-4 and 8-11. Please cancel claims 5-7. Upon entry of this amendment, claims 1-4 and 8-11 will be pending and under consideration. No new matter has been entered by way of these amendments.

Support for the amendment to claim 1 that requires the transplanted subject to be a kidney transplanted subject may be found in the examples, original claim 6 and on page 6 of the specification. Support for the amendment to claim 10 adding "hybridization technique" may be found at page 3, the first full sentence. Support for the addition of SEQ ID NOs:29-38 to the claims may be found in original Table 3, which is present at page 25 of U.S. Provisional Application No. 60/405,225 (from which the instant §371 application claims priority), and page 21 of PCT Application No. PCT/EP2003/009292 (from which the instant §371 application is a National Stage entry). Table 3 in both the provisional and international application sets forth the GenBank® Accession Numbers and gene names for ten exemplary nucleic acid sequences for use in the presently claimed methods. These nucleic acid sequences are additionally discussed at, e.g., pages 5-6 of the provisional application and page 6 of the international application. These GenBank® Accession Numbers are incorporated by reference at page 2 of the provisional application, and page 2 of the PCT Application. Accordingly, the introduction of these sequences does not constitute new matter. Applicants provide herewith a CRF and a paper copy of the current sequence listing, including newly-added SEQ ID NOs:29-38.

Claim 1. (Currently Amended) A method of early diagnosing chronic rejection (CR) in a kidney transplanted test subject, comprising: ~~subject comprising~~

a) ~~taking~~ detecting as a baseline value the level of mRNA expression corresponding ~~to~~ to, or protein encoded ~~by~~ by, the nucleic acid sequences set forth in SEQ ID NOs:29, 30, 31, 32,

33, 34, 35, 36, 37, and 38, ~~the gene~~ said nucleic acid sequences originating from a ~~specific~~ renal allograft tissue biopsy of a kidney transplanted control subject who is known not to develop CR;

b) detecting ~~a~~ as a test value the level of mRNA expression corresponding ~~to~~ to, or protein encoded ~~by~~ by, the ~~at least one gene identified~~ nucleic acid sequences selected in step a) in ~~an~~ a renal allograft tissue biopsy ~~of the same tissue type as in a)~~ obtained from a kidney transplanted test subject ~~patient~~ within the first year post-transplantation; and

c) comparing the ~~first~~ baseline value with the ~~second~~ test value, wherein a ~~first~~ baseline value lower than the test value, in the case of the nucleic acid sequences set forth in SEQ ID NO:29, 30, 31, 32, 33, 34, 35 or 36, and ~~or~~ higher than the ~~second~~ test value, in the case of the nucleic acid sequences set forth in SEQ ID NO:37 or 38, predicts that the kidney transplanted test subject ~~is at~~ has an increased risk of developing CR.

Claim 2. (Currently Amended) ~~A~~ The method according to claim 1, wherein the ~~baseline value a) is obtained by detecting a level of mRNA expression corresponding to or protein encoded by at least one gene in an~~ renal allograft tissue biopsy of the transplanted control subject is obtained from the ~~donor~~ control subject at the day of transplantation.

Claim 3. (Currently Amended) A method for monitoring CR in a kidney transplanted subject at risk of developing ~~CR comprising~~ CR, comprising:

a) obtaining a ~~pre-administration~~ sample from a kidney transplanted subject prior to administration of a ~~CR inhibiting agent,~~ CR-inhibiting agent;

b) detecting the level of expression of mRNA corresponding ~~to~~ to, or protein encoded ~~by the~~ by, ~~at least one gene~~ the nucleic acid sequences set forth in SEQ ID NOs:29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, in the ~~pre-administration sample,~~ sample obtained in step a);

c) obtaining ~~one or more post-administration samples~~ at least one sample from the kidney transplanted ~~patient,~~ subject after administration of a CR-inhibiting agent;

d) detecting the level of expression of mRNA corresponding ~~to~~ to, or protein encoded ~~by~~ by, the ~~at least one gene~~ nucleic acid sequences selected in ~~the post-administration sample or samples,~~ step b); and

e) comparing the level of expression of mRNA or protein detected in step b) and step d); ~~encoded by the at least one gene in the pre-administration sample with the level of expression of mRNA or protein encoded by the at least one gene in the post-administration sample or samples, and f) adjusting the agent accordingly.~~

, wherein an increase in the level detected in step d) in comparison to the level detected in step b) in the case of the nucleic acid sequences set forth in SEQ ID NOs:29, 30, 31, 32, 33, 34, 35 and 36, and a decrease in the level detected in step d) in comparison to the level detected in step b) in the case of the nucleic acid sequences set forth in SEQ ID NO: 37 and 38, provides a negative indication of CR in the kidney transplanted subject.

Claim 4. (Currently Amended) A method for preventing, inhibiting, reducing or treating CR in a kidney transplanted subject in need of such ~~treatment comprising~~ treatment, comprising administering to the subject a ~~compound~~ CR-inhibiting agent that modulates the synthesis, expression or activity of ~~one or more genes or gene products~~ the nucleic acid sequences set forth in SEQ ID NOs:29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 or the gene products encoded by the nucleic acid sequences set forth SEQ ID NOs:29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 ~~as identified in claim 1~~, so that at least one symptom of CR is ameliorated.

Claims 5-7. (Canceled).

Claim 8. (Currently Amended) ~~A~~ The method according to claim 1, wherein the baseline value and the test value are ~~level of expression of the gene expression is~~ assessed by detecting the ~~presence of a~~ levels of protein encoded by the nucleic acid sequences. ~~corresponding to the gene expression product.~~

Claim 9. (Currently Amended) ~~A~~ The method according to claim 8, wherein the ~~presence of the~~ levels of protein are ~~protein is~~ detected using reagents that ~~a reagent which~~ specifically bind ~~binds~~ to the ~~protein~~ proteins.

Claim 10. (Currently Amended) ~~A~~ The method according to ~~claim 1~~ claim 11, wherein the ~~level~~ levels of mRNA expression ~~of one or more genes is~~ are detected by ~~techniques selected from the group consisting of~~ Northern blot analysis, a hybridization technique, reverse transcription PCR ~~and~~ or real time quantitative PCR.

Claim 11. (Currently Amended) ~~A~~ The method according to claim 1, wherein the baseline value and the test value are assessed by detecting the levels ~~level~~ of mRNA expression corresponding to the nucleic acid sequences. ~~of a set of genes is detected.~~

Claims 12-14. (Canceled)